



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,779	04/20/2001	Amin I. Kassis	U0381-00001	2010
21874 7590 12/21/2007 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205			EXAMINER HANLEY, SUSAN MARIE	
			ART UNIT 1651	PAPER NUMBER
			MAIL DATE 12/21/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

**Application No.**

09/839,779

**Applicant(s)**

KASSIS ET AL.

**Examiner**

Susan Hanley

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 50-92 is/are pending in the application.
- 4a) Of the above claim(s) 56-58, 64-67 and 69-75 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 50-55, 59-63, 68 and 76-92 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### DETAILED ACTION

The remarks and amendments filed 2/20/07, 3/28/07 and 8/6/07 are acknowledged.

#### *Status of the Claims*

Claims 50-92 are pending. Claims 50-53 and 59-75 were subject to a specie election. On July 16, 2002, Applicant elected a gamma emitter for the R1 specie. Phosphatase and phosphate moiety were elected for the enzyme and prosthetic group, respectively. This specie combination remains under examination. Claims 56-58, 64-67, and 69-75, stand withdrawn from further examination.

The prior art rejections against claim 54 and the claims depending therefrom (55 and 76-92) were overcome by Applicant's arguments, see pages 8-12, filed 7/14/06 and indicated as allowable. However, new grounds of rejection based on 35 USC 112 are made in the Office action against these claims.

Claims 50-55, 59-63, 68 and 76-92 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### *Priority and Declaration*

Applicant has provided a new declaration which clarifies that the instant application claims benefit of prior-filed provisional application No. 60/199,350, filed 4/25/2000, under 35 U.S.C. 119(e). The previous declaration claimed priority 35 U.S.C. 119(e) and identified the title and date of the nonprovisional. However, the serial number for this provisional application was not identified. The declaration submitted on is accepted and the priority date for this application is April 25, 2000.

***Specification***

The amendment to specification submitted on 8/6/07 fulfills the requirement for a reference for priority to an unknown provisional application.

***Response to Amendment***

The declaration filed on 3/28/07 under 37 CFR 1.131 is sufficient to overcome the Ho et al. (ACS Meeting on April 1-5, 2001) reference.

***Claim Rejections - 35 USC § 112***

The rejection to claim 77 is rejected under 35 U.S.C. 112, second paragraph, is withdrawn in light of the amendment filed 8/6/07.

***Claim Rejections - 35 USC § 102***

The rejection of claims 50-53, 59-63 and 68 under 35 U.S.C. 102(a) as being clearly anticipated by Ho et al. (ACS Meeting on April 1-5, 2001) in light of Pero et al. (US 6,538,038) is withdrawn in light of the declaration filed on 3/28/07 under 37 CFR 1.131 and the establishment of the priority claim to the provisional application 60/199,350, filed 4/25/2000.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-55, 59-63, 68 and 76-92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

Art Unit: 1651

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment filed 7/9/04 introduced the phrase "substantially water-insoluble" to independent claims 23 (now cancelled), 50 and 54 to counter a rejection and discussion about precipitates and insolubility related to Hansen (US 5,851,527). However, the specification does not support a "substantially water-insoluble" drug entrapped in the extracellular space. The specification teaches "water-insoluble" and "high water-insoluble", but not "substantially water-insoluble". The term "substantially" broadens the meaning of water-insoluble, which is interpreted to mean not soluble in water. The specification fails to support the scope of the meaning "substantially water-insoluble" which is interpreted to mean mostly but not totally water-insoluble. In fact, the specification's reference to "high water-insoluble" teaches away from substantially water-insoluble". Therefore, the amendment of 7/9/04 introduced NEW MATTER into the claims because the specification as-filed does not contemplate nor disclose a broader concept of "not soluble in water". Hence, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

Claims 54, 76-84 and 91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 54 is drawn to a method for in vivo localization of a drug in the extracellular space of a tumor by cleaving the prosthetic group of a water-soluble prodrug that is administered to an animal. The claim further specifies that the enzyme is unique to the tumor or is produced at concentration that are higher than in normal tissues. Claim 60 defines the tumor-related enzymes.

Thus, the claims encompass the use of prodrugs that comprise a prosthetic group that are cleavable by the target enzyme for which no written description has been provided. Moreover, the sole example of using a radiolabelled X-gal, wherein prosthetic group is beta-D-galactosyl, phosphate, sulfate, amino acid or polypeptide, the does not provide a representative sample of prodrugs that can be cleaved by any tumor-associated enzyme encompassed by the claims, given the huge variation in physical, structural, and chemical properties of prodrugs encompassed by the current broad claim language. Because the claims encompass a multitude of prodrugs neither contemplated nor disclosed by the as-filed disclosure, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

Claims 50-55, 59-63, 68 and 76-92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 50 and 54 recite the phrase "wherein the enzyme is unique to tumor cells" which is held to be vague. It is unclear if the term "unique" means that the enzyme is unique in structure and expressed by the cell or if the term means "different" by virtue of possessing a property that other cells lack. For example, an exogenous enzyme-labeled antibody that attaches to a tumor cell modifies the tumor cell and makes it different and unique since an exogenous enzyme is now

Art Unit: 1651

attached to it. It is suggested that the claim be changed to "wherein the enzyme is produced only by the tumor cells".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Susan Hanley  
Patent Examiner  
AU 1651

SANDRA E. SAUCIER  
PRIMARY EXAMINER

